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| 10/538,038 | 06/08/2005 | Jay Patrick Slack | 102790-135 (30069 US/2) | 1345 |
| 27389 7590 09/24/2007 NORRIS, MCLAUGHLIN & MARCUS 875 THIRD AVE 18TH FLOOR NEW YORK, NY 10022 | | | EXAMINER LONG, SCOTT | |
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

| | | | |
|------------------------------|--------------------------------------|-------------------------------------|--|
| Office Action Summary | Application No. 10/538,038 | Applicant(s) SLACK ET AL. | |
| | Examiner Scott D. Long | Art Unit 1633 | |

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 16 July 2007.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1,2 and 5-13 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1,2 and 10-13 is/are rejected.
- 7) ☒ Claim(s) 5-9 is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

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DETAILED ACTION

The examiner acknowledges receipt of Applicant's Remarks and Claim amendments on 19 July 2007.

Claim Status

Claims 1, 5-9, and 13 are amended. Claims 1-2 and 5-13 are under current examination.

Priority

This application claims benefit as a 371 of PCT/CH03/00830 (filed 12/17/2003) which claims benefit of 60/434,790 (filed 12/18/2002). The instant application has been granted the benefit date, 18 December 2002, from the application 60/434,790.

Claim Objections

Claims 5-8 are objected to because of the following informalities: The claims contain the word, "SEQ ID". In order to comply with the sequence rules, these should be rewritten as "SEQ ID NO:." See MPEP 2422; 37 CFR 1.821(2)(d). Appropriate correction is required.

Response to Arguments - Claim Rejections 35 USC § 112

Response to Arguments – 35 USC 112, second paragraph

Applicant's arguments, see page 4 and Claim amendments, filed 19 July 2007, with respect to claim 13 has been fully considered and is persuasive. The rejection of Claim 13 under 35 USC 112, second paragraph, has been made moot by the claim amendments submitted on 19 July 2007 and is hereby withdrawn.

Response to Arguments – 35 USC 112, first paragraph

Applicant's arguments, see page 4 and Claim amendments, filed 19 July 2007, with respect to claims 14-15 has been fully considered and is persuasive. The rejection of Claims 14-15 under 35 USC 112, first paragraph, has been made moot by the cancellation of claims 14-15 submitted on 19 July 2007 and is hereby withdrawn.

Response to Arguments - Claim Rejections 35 USC § 103

Applicant's arguments, see pages 4-11, and Claim Amendments, filed 19 July 2007, have been fully considered and they are found to be persuasive.

Therefore, the examiner hereby withdraws the rejection of claims 1-6 and 9-17 as being obvious over Margolskee (US-5,817,759) in view of Yao et al. (US-7,041,457).

NEW GROUNDS OF REJECTION

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-2, and 10-13 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The methodology for determining adequacy of Written Description to convey that applicant was in possession of the claimed invention includes determining whether the application describes an actual reduction to practice, determining whether the invention is complete as evidenced by drawings or determining whether the invention has been set forth in terms of distinguishing identifying characteristics as evidenced by other descriptions of the invention that are sufficiently detailed to show that applicant was in possession of the claimed invention (*Guidelines for Examination of Patent Applications under 35 USC § 112, p 1 "Written Description" Requirement*; (Federal Register/Vol 66, No. 4, Friday, January 5, 2001; II Methodology for Determining Adequacy of Written Description (3.)).

Claim 1 is broadly drawn, such that it applies to any a genus of $G_{\alpha q}$ -Gustducin chimeric G-protein wherein the last 44 amino acids of the $G_{\alpha q}$ protein sequence are replaced with a 44 amino acid unit of Gustducin. However, the working examples provided in the instant application only demonstrate individual species of $G_{\alpha q}$ -Gustducin chimeric G-protein, specifically SEQ ID NO:2.

Although the specification has support for the claim language of the newly amended claim 1, "In a further specific embodiment the G-protein is one wherein at least the last 5 amino acids of the G, are replaced by a corresponding number of amino acids of Gustducin, more particularly the last 44 amino acid sequences of the $G_{\alpha q}$, is replaced with a 44 amino acid unit of Gustducin." (page 4, last paragraph), the specification does not define which 44 amino acids of Gustducin can be used to replace the C-terminus of the G protein. Furthermore, the specification fails to adequately describe the important structural features of the 44 amino acid substitution which are required for the gustatory activity of the $G_{\alpha q}$ -Gustducin chimeric G-protein described in the specification.

The Revised Interim Guideline for Examination of Patent Applications under 35 USC § 112, p1 "Written Description" Requirement (Federal Register/ Vol 66. No 4, Friday January 5, 2001) states "THE CLAIMED INVENTION AS A WHOLE MAY NOT BE ADEQUATELY DESCRIBED IF THE CLAIMS REQUIRE AN ESSENTIAL OR CRITICAL ELEMENT WHICH IS NOT ADEQUATELY DESCRIBED IN THE SPECIFICATION AND WHICH IS NOT CONVENTIONAL IN THE ART" (column 3, page 71434), "WHEN THERE IS SUBSTANTIAL VARIATION WITHIN THE GENUS, ONE MUST DESCRIBE A SUFFICIENT VARIETY OF SPECIES TO REFLECT THE VARIATION WITHIN THE

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GENUS", "IN AN UNPREDICTABLE ART, ADEQUATE WRITTEN DESCRIPTION OF A GENUS WHICH EMBRACES WIDELY VARIANT SPECIES CANNOT BE ACHIEVED BY DISCLOSING ONLY ONE SPECIES WITHIN THE GENUS" (column 2, page 71436, emphasis added).

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states that "APPLICANT MUST CONVEY WITH REASONABLE CLARITY TO THOSE SKILLED IN THE ART THAT, AS OF THE FILING DATE SOUGHT, HE OR SHE WAS IN POSSESSION OF THE INVENTION. THE INVENTION IS, FOR PURPOSES OF THE 'WRITTEN DESCRIPTION' INQUIRY, *WHATEVER IS NOW CLAIMED*." (See page 1117). The specification does not "clearly allow persons of ordinary skill in the art to recognize the [he or she] invented what is claimed." (See *Vas-Cath* at page 1116).

One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481, 1483. In *Fiddes*, claims directed to mammalian FGF's were found to be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence.

Considering the potentially large numbers of polypeptides encompassed by these claims, the disclosure is not sufficient to show that a skilled artisan would recognize that the applicant was in possession of the claimed invention (genus) commensurate to its scope at the time the application was filed.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-2, and 10-13 are rejected under 35 U.S.C. 103(a) as being obvious over Margolskee (US-5,817,759, issued 6 October 1998) in view of Yao et al. (US-7,041,457, issued 9 May 2006) and further in view of Ruiz-Avila et al. (PNAS. July 17 2001. vol.98; No.15: 8868-8873).

Claim 1 is directed to a $G_{\alpha q}$ -Gustducin chimeric G-protein wherein the last 44 amino acids of the $G_{\alpha q}$ protein sequence are replaced with a 44 amino acid unit of Gustducin. Claim 1 is broadly drawn such that the chimeric G-protein comprises a 44 amino acid sequence of Gustducin, but the particular 44 amino acid sequence is not specified.

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Margolskee teaches "the α subunit of a novel taste receptor cell specific G protein, gustducin, or fragments and variants of the α subunit" (col. 3, lines 3-5). Margolskee teaches, "Gustducin α subunit variants...may comprise polypeptide analogs wherein one or more of the specified amino acids is deleted or replaced or wherein one or more nonspecified amino acids are added" (col.3, lines 48-51). Yao et al. teach that a preferred embodiment has "at least about five amino acids in the C terminus of the G_q -protein replace by at least about five amino acids from the C terminus of $G_{\alpha_{olf}}$ or transducin" (col.5, line 16-19) and "up to 44 amino acids of the C terminus of transducin or $G_{\alpha_{olf}}$ may be incorporated" (col.5, lines 22-23). Yao et al. indicated that the C-terminus of $G\alpha$ proteins can be modified to promote promiscuity of taste receptors. Yao et al. also describe the shared homologies of $G\alpha$ subunits. Further, Yao et al. also suggest that the gustducin-coupled bitter receptor can be modified to increase promiscuity with regard to GPCR coupling (col.4, lines 35-55). In particular, Yao et al. show that their chimeric G-protein wherein the C terminus of the G_q -protein is replaced by 44 amino acids of transducin has functional activity with the Taste Receptor (col.8, Table I, and Examples). Ruiz-Avila et al. teach, "Several biochemical studies suggest that the interaction of gustducin with its cognate taste receptors is similar to that of transducing with rhodopsin. A key result of these studies is that the C terminus of α -gustducin is a critical determinant for its interaction with taste receptors" (page 8870, col.1, Results). Consequently, claim 1 would be obvious, in light of the teachings of Margolskee and Yao et al. and Ruiz-Avila et al.

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Claim 2 is directed to the chimeric protein of claim 1, wherein the G-protein is a $G_{\alpha 15}$ or 16 -Gustducin. Margolskee teaches, $G_{\alpha 15}$ and $G_{\alpha 16}$ (col.2, line 4).

Claim 10 is directed to methods of producing a chimeric G-protein of claim 1 by recombinant technology. Margolskee teaches, "large scale production of gustducin α subunit polypeptides" by recombinant methods (col. 3, line 24-35). Margolskee teaches stably transformed host cells comprising the expression vector (col.3, line 24).

Claim 11 is directed to a method of analysis and discovery of modulators of bitter taste receptors using the chimeric proteins of claim 1. Margolskee teaches, "methods for identifying taste modifying agents having the capability to affect interactions between the gustducin α subunit and taste receptors or effectors and also describes methods for utilizing such taste modifying agents to modify taste by mimicking or inhibiting...bitter." (col. 4, lines 52-56).

Claims 12-13 directed to a method of claim 11, wherein the assay is a mammalian cell-based assay. Margolskee teaches such mammalian cell-based assays that measure changes in intracellular messengers, including phosphodiesterase (col.13, lines 4-21) which affects Ca^{2+} and IP3 production.

Margolskee does not specifically teach the $G_{\alpha q}$ -Gustducin chimeric G-protein and also does not specifically recited replacement of the C-terminal sequence 44 amino acids of the gustducin receptor.

Yao et al. teach, $G_{\alpha q}$ chimeric G-proteins (col.4, lines 12-27). In particular, the chimeric proteins described, combine various $G_{\alpha q}$ class proteins. Yao et al. also teach

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chimeric G-proteins that comprise C-terminal sequences from Transducin and $G_{\alpha_{olf}}$ (col3, lines 12-13).

Yao et al. also teach analysis and discovery of agonists and antagonists of chemosensory receptors, using G_q -protein variants (col.3, lines 15-30), including the "gustducin-coupled bitter receptor" (col.4, line 53). Yao et al. further suggest that modulators could be used in "protein pharmaceutical and food industries" (col.4, line 32). Yao et al. teach that a preferred embodiment has "at least about five amino acids in the C terminus of the G_q -protein replace by at least about five amino acids from the C terminus of $G_{\alpha_{olf}}$ or transducin" (col.5, line 16-19) and "up to 44 amino acids of the C terminus of transducin or $G_{\alpha_{olf}}$ may be incorporated" (col.5, lines 22-23). Consequently, claims 3-4 would be obvious, in light of the teachings of Yao et al.

Ruiz-Avila et al. teach the nexus of gustducin and transducing homology and the importance of the C-terminus for interacting with taste receptors.

It would have been obvious to the person of ordinary skill in the art at the time of the invention was made to make a G_{α_q} -Gustducin chimeric G-protein having a 44 amino acid substitution from Gustducin.

The person of ordinary skill in the art would have been motivated to make this protein because, "C-terminal substitution increases promiscuity of said variant G_q protein as compared to the corresponding native G_q protein" (Yao et al. col.5, lines 20-22). While Yao et al. does not specifically teach making a chimera between G_q protein and gustducin, it is clearly obvious in light of the teachings involving substitutions with C-terminal sequences from other chemosensory molecules, transducin and $G_{\alpha_{olf}}$. In

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particular, Yao et al. show that their chimeric G-protein wherein the C terminus of the G_q -protein is replaced by 44 amino acids of transducin has functional activity with the Taste Receptor (col.8, Table I, and Examples). Ruiz-Avila et al. teach, "Several biochemical studies suggest that the interaction of gustducin with its cognate taste receptors is similar to that of transducing with rhodopsin. A key result of these studies is that the C terminus of α -gustducin is a critical determinant for its interaction with taste receptors" (page 8870, col.1, Results). Furthermore, Yao et al. suggest that analysis and discovery of agonists and antagonists of chemosensory receptors, using G_q -protein variants can be performed using chimeric proteins and actually mention gustducin bitter receptor as a receptor which might be useful "to customize sensory perception" (col.4, line 32-33).

An artisan would have expected success, because Yao et al. were successful in making similar chimeric G-proteins with other chemosensory receptors.

Therefore the products and method as taught by Margolskee in view of Yao et al. and further in view of Ruiz-Avila et al. would have been *prima facie* obvious over the method of the instant application.

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Allowable Subject Matter

Claims 5-9 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

No claims are allowed.

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Examiner Contact Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to **Scott Long** whose telephone number is **571-272-9048**.

The examiner can normally be reached on Monday - Friday, 9am - 5pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, **Joseph Woitach** can be reached on **571-272-0739**. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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Art Unit 1633

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JLE